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10/553,100	10/13/2005	Takayuki Oka	Q90338	2227

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EXAMINER	
HAQ, SHAFIQUL	
ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,100	OKA ET AL.	
	Examiner	Art Unit	
	SHAFIQUL HAQ	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-8 and 10-28* is/are pending in the application.

4a) Of the above claim(s) *18-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-8, 10-17, 27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' amendments and remarks filed 9/27/08 is acknowledged and entered.

2. Claims 2-8, 10-17, 27 and 28 are under active prosecution.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 2-8, 10-17, 27 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "magnetic substance-encapsulated particle, which comprises an organic polymer material and a magnetic substance" in lines 1-2 and also recites "the magnetic substance being contained within a particle" in lines 4-5. The composition of "a particle" is unclear because it is unclear whether the particle is comprised of the organic polymer material or the composition of "an organic polymer and a magnetic substance" is contained within "a particle", which is of different composition.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 2-8, 10-14 and 27 are again under 35 U.S.C. 103(a) as being unpatentable over Kasai *et al* (US 5,814,687) in view of Wang *et al* (US 5,283,079) and further in view of Chandler *et al* (US 6,773,812).

Kasai discloses magnetic polymer particles that are configured by incorporating a magnetic substance into an organic polymer material (see abstract and summary of invention) and the magnetic polymer particle being characterized in that the number average particle diameter of the magnetic polymer particles is generally 0.02-10μM (column 9, lines 24-25), which overlaps with the range of particle size of 1-30 nm of instant claim 2. Kasai also discloses that the magnetic substance is homogeneously dispersed throughout the center of the magnetic polymer particles (column 15, lines 12-15; column 6, lines 36-37 and column 8, lines 4-7 and 44-45), which reads on the phrase “magnetic substance being contained within a particle in a state of being dispersed" as recited in claim 2.

Kasai discloses different components ratio between the organic polymer content and the magnetic substance content (columns 4-9) and disclose preparation of magnetic polymer particles with different polymer magnetic substance ratios to obtain magnetic polymer particles having uniform particle with desired dispensability of magnetic substance, but fail to disclose a range of 0.3 or less for the absolute deviation in the content ratio of the magnetic material throughout the magnetic particles.

Wang discloses use of magnetic particle having uniform size distribution and magnetic content useful in immunoassays and for a wide variety of biomedical

applications (column 2, lines 8-10; claims 1, 9, 17 and 25). Wang also discloses that the magnetic particles can be optimized in terms of magnetic substance content for a wide variety of biomedical applications (column 5, lines 65-67).

Chandler *et al* teach magnetic particle with desired magnetic response for separation and analytical assays of biomolecules. Chandler teaches that separation and analysis can be effected based on the variable degree of magnetic content of the particle (see abstract). Chandler further teaches controlling magnetic content associated with the core particle for providing particles having different magnetic response and making particle having a desired magnetic response by choosing particles both by size and magnetic content (column 4, lines 1-28).

Therefore, since it is common and known in the art of magnetic polymer particle to attempt to configure so that the magnetic particles have a uniform magnetic content to be useful for immunoassays and for a wide variety of biomedical applications (Wang and Chandler), it would be obvious to one of ordinary skill in the art at the time of the invention to configure the magnetic polymer particle of Kasai so that the magnetic polymer particle has a uniform content of magnetic substance (and so uniform content ratio) throughout the magnetic polymer particles, as appropriate, with the expectation for use in a variety of biomedical applications. In addition, delimiting a range of 0.27 or less for the absolute deviation in the content ratio of the magnetic material throughout the magnetic particles is viewed as a routine optimization, which can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art to discover an optimum value of

a result effective variable. "[W]here the general conditions of claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 223, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable is a known process is ordinary within the skill of the art." Application of Boesch, 617 F.2d 272,276,205 USPQ 215, 218-219 (C.C.P.A. 1980).

With regard to claim 3, the claim refers to the product of claim 2, which is produced by a particular process. For product by process claim see MPEP 2113. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). In this case, the magnetic particle of Kasai in view of Wang as described above would have the same charateristics as the magnetic substance-encapsulated particle of claim 2 (i.e. the product) that is obtained by the product by process claim of 3. However, as to the process, Kasai discloses oxidation of an iron compound in a polymerization process to prepare magnetic polymer particles (column 1, lines 45-51). As to claim 4, Kasai discloses magnetic polymer particles comprising iron (column 5, lines 60-

65 and column 9, lines 5-15). As to claim 5, Kasai discloses magnetic polymer particle comprising more than 50% by weight of (meth)acrylate (see abstract) and the thus the main constituent of the organic polymer particle is polymer comprising an acrylic monomer. As to claim 6, Kasai discloses monomer glycidyl methacrylate (column 7, lines 14-15). With regard to claim 7, Kasai discloses magnetic polymer particles comprising copolymer of acrylic monomer, vinyl monomer and monomer unit containing unsaturated carboxylic acid (column 3, lines 25-54) and disclose that the monomers include glycidyl methacrylate (column 7, lines 14-15) and styrene (column 5, lines 24-27). With regard to proportion of styrene monomer in the polymer (as claimed in claim 8), Kasai discloses different proportions of different monomers in the polymer composition (see polymer compositions of columns 3-7). However, as evidenced from the wide range (5-90% by weight) requirement, the proportion of the monomer units does not seem to be critical to the practice of the invention and a particular working condition can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art to discover an optimum value of a result effective variable. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). “No invention is involved in discovering optimum ranges of a process by

routine experimentation." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable is a known process is ordinary within the skill of the art." Application of Boesch, 617 F.2d 272,276,205 USPQ 215, 218-219 (C.C.P.A. 1980).

With regard to claim 10, Kasai discloses that magnetic polymer particles including a magnetic substance can be prepared by polymerizing hydrophobic cross-linking monomers (column 2, lines 46-48). With regard to claim 11, polymer particles having a specific functional group (column 1, lines 45-47) and teaches that the magnetic polymer particle comprises ethylenically unsaturated carboxylic acid (column 4, lines 1-3). Further, Kasai discloses ethylene glycol dimethacrylate (column 7, line 20) as a component that constitutes the polymer, which is a bifunctional crosslinkable monomer and therefore, the polymer that is disclosed therein can be considered to be a crosslinked polymer. In addition, styrenesulfonate (column 7, lines 6-7) is used as the vinyl monomer that constitutes the polymer; therefore, it can be expected that sulfonic acid groups are present on the surface of the polymer in question. As to claim 12, Kasai discloses number average particle diameter of magnetic polymer particle is generally 0.02 to 10μM preferably 0.5 to 5μM (lines 24-26 of column 9), which overlaps with "average particle size of 0.05 to 1μM" of instant claim 12. As to claim 13, Kasai discloses that proportion os supermagnetic substance in the magnetic polymer particles is preferably 1-100 parts by weight, more preferably by 5-80 parts by weight by 100 parts by weight of acrylate polymer and a particularly preferred proportion of the supermagnetic

substance is 10-60% parts by weight (column 7, lines 40-54), which overlaps with 0.1 to 50% by weight of the magnetic substance content of the magnetic substance-encapsulated particle of instant claim 13. As to claim 14, Kasai discloses that particle diameter of supermagnetic substance constituting magnetic polymer particle is preferably 40-300Å (i.e. 4-30nm), more preferably 50-200 Å (i.e. 5-20nm) and particularly preferably 60-150 Å (i.e. 6-15 nm) (line 66 of column 5 to line 10 of column 6), which overlaps with particle size of magnetic substance of 2 to 10nm of instant claim 14. It is noted that in the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990).

With regard to claim 27, Kasai discloses that vinyl monomer unit (C) can be polymerized with monomers A (acrylic monomer) and B (monomer unit containing unsaturated carboxylic acid) and the monomer C may be ethylene glycol (meth)acrylate, diethylene glycol (meth)acrylate or polyethylene glycol (meth)acrylate (column 5, lines 24-36). Kasai does not disclose the number of ehtylene oxide repeat in the polyethylene glycol (meth)acrylate but compounds differing regularly by the successive addition of the same chemical group (e.g., by -CH2CH2O- repeat groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977) ((MPEP § 2144.08) and thus different number of repeat groups would be obvious absent unexpected results.

7. Claims 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kasai *et al* (US 5,814,687) in view of Wang *et al* (5,283,079) and Chandler *et al* (US 6,773,812) as described above and further in view of Noetzel *et al* (US 4,568,706).

See the above teaching of a magnetic substance of Kasai *et al* in view of Wang *et al* and Chnadler *et al*. Kasai further teaches that biologically active materials such as antibodies, antigens etc. can be combined with the magnetic polymer particles and either a chemical bonding method or a physical adsorption method can be used for immobilizing the biological materials (column 13, lines 53-67 and claim 8 of Kasai). Kasai *et al* further teaches that magnetic polymer of their invention can be used as a carrier of biologically active materials such a protein, nucleic acid, enzymes etc. (Abstract and column 14, lines 7-13).

Kasai *et al* however, fail to teach a linker for linking the biologically active substance to the carrier through a linker.

Noetzel *et al* disclose cross-linked bead polymer and teaches that the cross-linked bead polymer can be used as carriers of biologically active substance (column 6, lines 12-15) wherein a spacer (e,g, bifunctional linkers) is preferably used for linking the biologically active substance to the polymeric beads. Noetzel et al teach that preferable spacer include as those which introduce epoxide group such as ethylene glycol diglycidyl ether. (line 66 of column 8 to line 14 of column 9). Noetzel et al further discloses that polymers containing epoxide groups which thus obtained using the linkers have a considerable higher activity that other products obtained

direct polymerization of monomers containing epoxide groups (column 9, lines 30-35).

Therefore, given the fact that biologically active substance can be linked to polymer containing beads by use of a spacer (i.e. a linker), preferably with bifunctional ethylene glycol diglycidyl ether linker which introduces epoxide groups and given the fact that epoxide groups so introduced provides polymer containing epoxide groups that are considerably more reactive than polymer beads wherein functional groups are introduced by direct polymerization of monomers, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a linker such as the ethylene glycol diglycidyl ether inker as though by Noetzel *et al* to link the biologically active substance to polymer encapsulated magnetic particle of Kasai *et al*, with the expectation of producing polymer encapsulated magnetic particle having epoxy group that are more reactive for linking the biologically active substance.

With regard to formation of covalent bond formation with antigen or an antibody (as claimed in claim 15 and 16), the epoxide group is capable of forming covalent bond with biologically active substance (column 3, lines 8-10) and with regard to claim 17, Noetzel *et al* as descrived above disclose ethylene glycol diglycidyl ether as a linker to link biologically active substance to polymeric substance.

8. Claims 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kasai *et al* (US 5,814,687) in view of Wang *et al* (5,283,079) and Chandler *et al* (US 6,773,812)

as described above and further in view of Ko *et al* (JP 2003012709 and pages 18-21 of STN search).

See the above teaching of a magnetic substance encapsulated particle of Kasai *et al* in view of Wang *et al* and Chandler *et al*. Kasai further teaches that the magnetic particle of the invention can be used as a material for magnetic toner and magnetic inks (column 14, lines 7-13 of Kasai)

Kasai *et al* in view of Wang *et al* fail to teach that the magnetic substance encapsulated polymer comprises a compound represented by general formula (2) as claimed in claim 2.

Ko *et al* disclose microparticles comprising resins from vinylic and acrylic monomers wherein the resins include a monomer (see page 19 of STN search, RN 140651-97-4) having a formula that reads on the compound of formula (2). Ko *et al* further disclose that the microparticles having the resin composition can be used in applications as ink and ink-jet recording devices and the resin composition provides particle with good stability (see title and abstract and pages 18 of STN search).

Therefore, it would be obvious to one of ordinary skill in the art at the time the invention was made to include the monomers of Ko *et al* in the polymeric composition of Kasai *et al* with the expectation of providing magnetic substance particle with good stability useful in applications as ink, because Kasai et al envisioned using the magnetic particle as toner and as inks and Ko *et al* teaches that the polymeric composition provides good stability to the particles.

Response to argument

9. Applicant's arguments filed 9/29/08 have been fully considered, but are not persuasive to overcome the rejections under 35 USC 103. However, a further review of the claims necessitated new ground of rejections, which are described in this office action.

Applicants argued that Kasai does not teach or suggest the relevant feature as defined in pending claim 2, where the absolute deviation of a component ratio between a carbon element comprising the organic polymer material and a metal element composing the magnetic substance is 0.27. Applicants argued that Kasai is silent of absolute deviation and its effects on the specificity of immunoassays. With regard to Wang, Applicants argued that although Wang suggests that magnetic particles can be optimized in terms of size, surface area, metal oxide content, and surface characteristics, Wang is silent aboaut the optimization of the absolute deviation of the ratio of carbon to magnetic substance and accordingly Wang adds nothing to Kassai that would render calims 2-8, 10-14 and 27 obvious under 35 USC 103 (a).

With regard to Wang, Wang discloses use of magnetic particle having uniform size distribution and magnetic content useful in immunoassays (column 2, lines 8-10) and also teaches that fluorescence intensity of magnetic particles can be adjusted by varying magnetic metal oxide content (column 2, lines 2-4). Wang *et al* further teach optimization of magnetic particle in terms of magnetic content (column 5, lines 67). Chandler *et al*, as described in the rejection of this office action teach magnetic particle with desired magnetic response for separation and analytical

assays of biomolecules. Chandler teaches that separation and analysis can be effected based on the variable degree of magnetic content of the particle (see abstract). Chandler further teaches controlling magnetic content associated with the core particle for providing particles having different magnetic response and making particle having a desired magnetic response by choosing particles both by size and magnetic content (column 4, lines 1-28).

As to the rejections under 35 USC 103, Applicants must realize that one cannot show nonobviousness by attacking references individually wherein the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merk* & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fines*, 837 F.2d 1071, 5USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992). In this case Kasai discloses different components ratio between the organic polymer content and the magnetic substance content (columns 4-9) and disclose preparation of magnetic polymer particles with different polymer magnetic substance ratios to obtain magnetic polymer particles having uniform particle with desired dispensability of magnetic substance and Wang discloses use of magnetic particle having uniform size distribution and magnetic content useful in immunoassays and for a wide variety of

biomedical applications (column 2, lines 8-10; claims 1, 9, 17 and 25). Wang also discloses that the magnetic particles can be optimized in terms of magnetic substance content for a wide variety of biomedical applications (column 5, lines 65-67). Therefore, configuration for discovering an optimum value of the magnetic polymer particle of Kasai so that the magnetic polymer particle has a uniform content of magnetic substance (and so uniform content ratio) throughout the magnetic polymer particles with the expectation for use in a variety of biomedical applications in view of Wang would be obvious to one of ordinary skill in the art . "[W]here the general conditions of claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 223, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation.

Applicants further argued that "an absolute deviation of a component ratio between a carbon element comprising the organic polymer material and a metal element composing the magnetic substance is 0.7 or less" have proven critical to achieving remarkable, unexpected results in an immunoassay. Applicants cited comparative Example 1 and 4 for this. However, the change in immunoassay results cannot be directly linked to absolute deviation because various other factors such as polymer composition also play important roles. As for example, organic polymers used in examples 1-3 are of different composition than the organic polymers used in examples 15-18. Particles of example 1-3 comprises GMA, EGDM, AAm and PE-90 in different combinations (see table 1) but particles of examples 15-18 comprises

polymer of different composition (at least with respect to styrene and different concentration of other monomers). Further, size of the particles is different as well. Therefore, particles having different organic polymers and of different sizes are expected to behave differently with different ligands and thus the immunoassay results and therefore, immunoassy results as argued by Applicants are not directly attributable to the absolute deviation of a component ratio between a carbon element composing the organic polymer meterial and a metal element composing the magnetic substance of 0.27 or less".

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiqul Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shafiqul Haq/
Examiner, Art Unit 1641